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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No: 40072-0003

Applicant(s): Kazumi YAMAMOTO *et al.*

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Appl. No.: 10/681,192

Group Art Unit: 1625

Filing Date: October 9, 2003

Examiner: To be assigned

Title: HALOGEN-SUBSTITUTED QUINOLINE DERIVATIVES AND ECTOPARASITE CONTROL AGENT

DECLARATION UNDER 37 C.F.R § 1.132

We, Kazumi Yamamoto, Kazuhiko Oyama, Masayo Sakai, and Ryo Horikoshi, do hereby declare as follows:

1. We are the inventors of the captioned application and we understand the English language.

2. We understand that the claims in the captioned application have been rejected over Minowa *et al.* (U. S. patent No. 5,190,952).

3. We submit this declaration, based on our personal knowledge and additional experimental evidences, to explain that the control effect of quinoline derivatives of the present invention against ectoparasite is unexpectedly better than that obtained by using the compounds of Minowa *et al.*

4. We refer to our declaration of April 13, 2005 and reiterate that the claimed compounds are unexpectedly and vastly superior in exterminating the ectoparasites. For example, compounds 2 and 19 can exterminate more than 97% of the ectoparasites *verses* Minowa compounds C3 to C5, which exterminate only 20% of the ectoparasites (see Exhibit 1, Test 2). In another test (see Exhibit 1, Test 4). Minowa compounds C1 to C3 completely failed to exterminate the ectoparasites. The comparative study clearly indicates that the control effect against ectoparasites of the instant compounds are significantly superior than that of the Minowa compounds (see Exhibit 1). Therefore, the claimed compounds having substitutions at any two of the 5-

position to 7-position on the quinoline ring provided unexpected results and are superior compounds to control ectoparasites.

5. In addition, we submit the following experimental data (see Exhibit 2) comparing the control effect of a quinoline derivative according to the instant invention and that of the compounds of Minowa *et al.*:

Compounds 1, 2, 19 and 25 of the present invention were prepared according to the original specification. Compounds C6 to C8 of Minowa *et al.* were prepared according to the Minowa *et al.* disclosure, for comparative tests. In the comparative tests, compound C6 is the closest one to compound 13 of Minowa, which the examiner has referred to. The compound C6 has the same chemical structure as the compound 13, except that a methyl group (-Me) in R^1 is replaced with a methyloxy group (-OMe). Compounds C6 to C8 were prepared by di-substitution of a fluorine atom at 6- and 8-positions, 5- and 8-positions and 5-and 7-positions, respectively, unlike the compounds of the present invention. According to the evaluation tests described in the instant specification, that is, Test 2 (Insecticidal effect against *Ctenocephalides felis*) and Test 4 (Miticidal effect against *Dermanyssus gallinae*), all the compounds were evaluated for comparison.

6. The comparative test results are attached herewith (see Exhibit 2). The results indicate that while Compounds 2 and 19 can exterminate more than 97% of ectoparasites in Test 2, Compound C8 can exterminate only 10% of ectoparasites. Compound 1 can exterminate the same level of ectoparasites as Compound 2 in Test 2. In Test 4, Compounds C6 and C7 completely failed to exterminate the ectoparasites. That is, the control effects against ectoparasites of the Compounds 1, 2, 19 and 25 of the instant invention are significantly superior than those obtained by using the Compounds C6 to C8 of Minowa *et al.* (see Exhibit 2).

7. Accordingly, the data shows that the substitutions at any two of the 5-position to 7-position on the quinoline ring unexpectedly result in an excellent control effect.

8. Based on the teachings of Minowa *et al.* one skilled in the art would not have any motivation to design a compound with 5,6-di-substituents or 6,7-di-substituents on the quinoline ring, because Minowa *et al.* is directed towards the substitution of a fluorine atom only at 6-position, and not at the 5- or 7- positions. Minowa *et al.* therefore do not teach or suggest that a compound having 5,6-di-substituents or 6,7-di-substituents can be superior in control effect against ectoparasites as compared to the compounds di-substituted or mono-substituted at any one of the 5 to 8 positions on the quinoline ring. In fact, Minowa *et al.* do not teach compounds that are effective against ectoparasites (see Minowa *et al.*, col. 2, lines 53-62, and col. 3, lines 40-56). Therefore, Minowa *et al.* disclosure cannot render the claimed invention obvious.

9. We hereby declare that all statements made herein of our own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

28 / 09 / 2005
Date

Kazumi Yamamoto
Kazumi Yamamoto

28/09/2005
Date

Kazuhiko Oyama
Kazuhiko Oyama

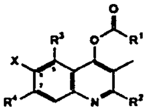
28/09/2005
Date

Masayo Sakai
Masayo Sakai

28/09/2005
Date

Ryo Horikoshi
Ryo Horikoshi

Exhibit 1: Comparative Test Results



(I)

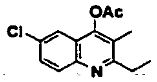
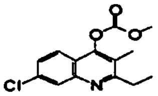
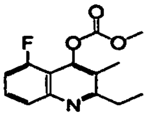
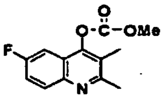
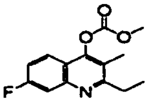
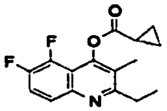
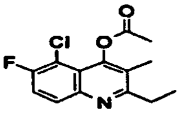
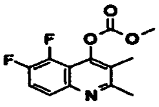
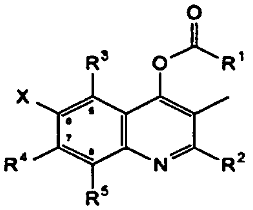
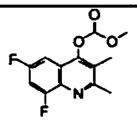
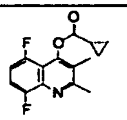
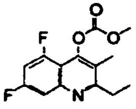
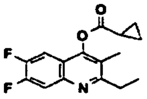
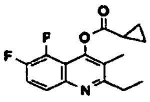
Compound No.	Structure	R^1	R^2	R^3	R^4	X	Test 2		Test 4	
							Insecticidal effect against *Ctenocephalides felis*		Miticidal effect against *Dermanyssus gallinae*	
							Conc. (ppm)	Death rate, %	Conc. (ppm)	Death rate, %
C1 (compound 22 of Minowa)		Me	Et	H	H	Cl	-	-	50	0
C2 (comparative)		-OMe	Et	H	Cl	H	-	-	50	0
C3 (comparative)		-OMe	Et	F	H	H	4	20	50	0
C4 (comparative)		-OMe	Me	H	H	F	4	20	-	-
C5 (comparative)		-OMe	Et	H	F	H	4	20	-	-
2 (the present invention)		c-Pr	Et	F	H	F	4	97	50	100
									20	97
19 (the present invention)		Me	Et	Cl	H	F	4	100	-	-
25 (the present invention)		-OMe	Me	F	H	F	-	-	50	100
									20	100

Exhibit 2: Comparative Test Results



(I)

Compound No.	Structure	R^1	R^2	position on the quinoline ring				Test 2		Test 4	
				5	6	7	8	Insecticidal effect against *Ctenocephalides felis*		Miticidal effect against *Dermanyssus gallinae*	
				R^3	X	R^4	R^5	Conc. (ppm)	Death rate, %	Conc. (ppm)	Death rate, %
C6 (comparative)		-OMe	Me	H	F	H	F	-	-	200	0
C7 (comparative)		c-Pr	Me	F	H	H	F	-	-	200	0
C8 (comparative)		-OMe	Et	F	H	F	H	4	10	-	-
1 (the present invention)		c-Pr	Et	H	F	F	H	20	100	-	-
2 (the present invention)		c-Pr	Et	F	F	H	H	4	97	50	100
								20	100	20	97